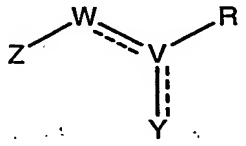
CLAIMS

1. A method of inhibiting dynamin-dependent endocytosis in cells, the method comprising treating the cells with an effective amount of a compound of formula I, or a physiologically acceptable salt thereof, wherein

M-Sp-M' **Formula I**

M and M' are each independently a moiety of formula II and are the same or different, and Sp is a spacer;



Formula II

V is C or CH;

W is CH or a linker group; and

Y is hydrogen, cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubsituted C_1-C_3 group or C_1-C_3 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the heterocyclic or carbocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C_1-C_3 group or C_1-C_3 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH_2R', CXR' or CHX'R';

X is O or S;

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubsituted C_1-C_3 group or C_1-C_3 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur;

R' is NH, O or S bonded to the spacer; and

Z is selected from:

(a) an unsubstituted heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S;

(b) an unsubstituted carbocyclic group consisting of one or two rings independently having 5 or 6 ring members;

(c) a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S wherein the heterocyclic group has one or more substituents independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl; and

(ii) a C_1-C_2 alkyl or C_1-C_2 alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl; and

(d) a carbocyclic group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents when W is CH or a linker group or W, V and Y form an unsubstituted carbocyclic group, or at least one substituent when W, V and Y form a heterocyclic group, independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl; and

(ii) a C_1-C_2 alkyl or C_1-C_2 alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl;

wherein when Z of one of M or M' is selected from (b), Z of the other of M or M' is selected from (a), (c) or (d).

2. A method according to claim 1 wherein:

V is C;

W is CH;

Y is hydrogen, cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C_1-C_2 group or C_1-C_2 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic

or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur, or an unsubstituted C_1-C_2 group or C_1-C_2 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH_2R', CXR' or CHX'R';

X is O or S; and

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C_1-C_2 group or C_1-C_2 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulphur.

3. A method according to claim 2 wherein:

Y is cyano, nitro, amino, carboxy, hydroxy, sulfhydryl, thiocarboxy, or a C_1-C_2 group substituted with a group selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy;

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carboxylic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy, or a C_1-C_2 group substituted with a group selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy; and

R is CXR'.

4. A method according to any one of claims 1 to 3 wherein Z is selected from:

(i) a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms independently selected from O, N and S;

(ii) a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms independently selected from O, N and S, wherein the heterocyclic group has one or more substituents independently selected from nitro, NH, halo, cyano, amino, hydroxy, carboxy, oxo, sulfur, and C_1-C_2 alkoxy; and

(iii) an carbocyclic group consisting of one or two rings independently

having 5 or 6 ring members, and at least two substituents independently selected from nitro, NH, amino, halo, cyano, hydroxy, carboxy, oxo, sulfur and C_1-C_2 alkoxy.

5. A method according to any one of claims 1 to 4 wherein Z of at least one of M and M' is other than a 2,3-disubstituted carboxycyclic group.

6. A method according to any one of claims 1 to 5 wherein Z of at least one of M and M' comprises:

at least two substituents in ortho positions relative to one another or in adjacent substitution positions, when the Z group is selected from (d) and W is CH or a C_1-C_3 linker group; or

the, or one of, the substituents on a carbon atom adjacent to the, or one of the, heteroatom(s) when the Z group is a heterocyclic group selected from (c); or

when W, V and Y are cyclised forming a heterocyclic ring fused with Z, the, or one of, the substituents on a carbon atom spaced at least one bond length from the heterocyclic ring.

7. A method according to any one of claims 1 to 6 wherein when the Y substituent of one of M or M' is hydrogen, the Y substituent of the other of M and M' is other than hydrogen.

8. A method according to any one of claims 1 to 7 wherein W, V and Y form a 5 or 6 membered heterocyclic ring fused with Z.

9. A method according to claim 8 wherein the heterocyclic ring fused with Z forms a two ring heterocyclic group.

10. A method according to any one of claims 1 to 8 wherein Z comprises an aryl group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents independently selected from nitro, NH, amino, halo, cyano, hydroxy, carboxy, oxo, sulphur and C_1-C_2 alkoxy.

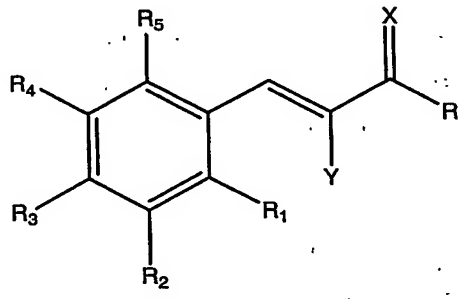
11. A method according to claim 10 wherein Z comprises an aryl group consisting of one ring having 6 ring members and at least two substituents independently selected from nitro, amino, halo, cyano, hydroxy, carboxy and C_1-C_2 alkoxy.

12. A method according to claim 11 wherein the aryl group has at least two substituents independently selected from nitro, amino, and hydroxy.

13. A method according to any one of claims 1 to 8 wherein Z comprises a heterocyclic group having one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S, wherein the heterocyclic group has one or more substituents independently selected from nitro, NH, halo, cyano, amino, hydroxy, carboxy, oxo, sulphur and C_1-C_2 alkoxy.

14. A method according to claim 13 wherein the heterocyclic group has one or more substituents independently selected from nitro, amino and hydroxy.

15. A method according to any one of claims 1 to 5 wherein M and M' are each independently a moiety as follows:



wherein:

X is O or S;

Y is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, or thiocarboxy; or

R_1 and Y are cyclised forming a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring, wherein the heterocyclic ring includes 1 or 2 heteroatoms selected from O,N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R_2 to R_5 are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, C_1-C_2 alkoxy and C_1-C_2 acyl; or

R_1 to R_5 are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, halo, C_1-C_2 alkoxy and C_1-C_2 acyl; and

R is NH, O is S bonded to the spacer Sp; and

wherein at least one of M and M' is characterised in that, at least two of R_1 to R_5 are other than hydrogen and when R_1 to R_2 are other than hydrogen at least one of R_3 to R_5 is also other than hydrogen, or when R_1 and Y are cyclised, at least two of R_2

to R_5 are other than hydrogen when R_1 and Y form an unsubsituted carbocyclic group or at least one of R_2 to R_5 is other than hydrogen when Y and R_1 form a heterocyclic group.

16. A method according claim 15 wherein R_1 to R_3 are other than hydrogen.

17. A method according to claim 15 wherein at least two of R_1 to R_5 are in ortho positions relative to one another.

18. A method according to claim 15 wherein at least one of M and M' has three substituents and wherein the substituents are adjacent to one another.

19. A method according to claim 18 wherein either R_1 to R_3 are other then hydrogen or R_2 to R_5 are other than hydrogen.

20. A method according to claim 15 wherein when at least one of R_1 to R_5 or R_2 to R_5 is halo, C_1-C_2 alkoxy or C_1-C_2 acyl, at least one other substituent is selected from nitro, amino, hydroxy, carboxy and thiorcarboxy when R_1 and Y are cyclised and form a heterocyclic ring, or at least two other substituents are selected from nitro, amino, hydroxy, carboxy and thiocarboxy when R_1 and Y are not cyclised or form an unsubstituted carboxylic ring.

21. A method according to any one of claims 15 to 20 wherein Y is cyano, X is O and R is NH.

22. A method according to any one of claims 1 to 21 wherein M and M' are the same.

23. A method according to any one of claims 1 to 22 wherein the spacer Sp permits the compound to adopt a hairpin conformation.

24. A method according to any one of claims 1 to 23 wherein the spacer Sp comprises an unsubstituted alkane chain as follows:

$$-CH_2(CH_2)_nCH_2-$$

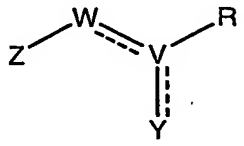
wherein n is an integer of from 1 to 5.

25. A method according to any one of claims 1 to 24 wherein the compound of Formula I is a dimeric tyrphostin.

26. A method of prophylaxis or therapeutic treatment of a disease or condition in a mammal mediated by dynamin-dependent endocytosis, the method comprising administering to the mammal an effective amount of a compound of Formula I, or a physiologically acceptable salt, or prodrug thereof, wherein:

M-Sp-M' **Formula I**

M and M' are each independently a moiety of formula II and are the same or different, and Sp is a spacer;



Formula II

V is C or CH;

W is CH or a linker group; and

Y is hydrogen, cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubsituted C_1-C_3 group or C_1-C_3 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the heterocyclic or carbocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C_1-C_3 group or C_1-C_3 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH_2R', CXR' or CHX'R';

X is O or S;

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubsituted C_1-C_3 group or C_1-C_3 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur;

R' is NH, O or S bonded to the spacer; and

Z is selected from:

(a) an unsubstituted heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S;

(b) an unsubstituted carbocyclic group consisting of one or two rings independently having 5 or 6 ring members;

(c) a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S wherein the heterocyclic group has one or more substituents independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl; and

(ii) a C_1-C_2 alkyl or C_1-C_2 alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl; and

(d) a carbocyclic group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents when W is CH or a linker group or W, V and Y form an unsubstituted carbocyclic group, or at least one substituent when W, V and Y form a heterocyclic group, independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl; and

(ii) a C_1-C_2 alkyl or C_1-C_2 alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl;

wherein when the Z group of one of M or M' is selected from (b), the Z group of the other of M or M' is selected from (a), (c) or (d).

27. A method according to claim 26 wherein:

V is C;

W is CH;

Y is hydrogen, cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C_1-C_2 group or C_1-C_2 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3

heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur, or an unsubstituted C_1-C_2 group or C_1-C_2 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH_2R', CXR' or CHX'R';

X is O or S;

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C_1-C_2 group or C_1-C_2 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R' is NH, O or S bonded to the spacer.

28. A method according to claim 27 wherein:

Y is cyano, nitro, amino, carboxy, hydroxy, sulfhydryl, thiocarboxy, or a C_1-C_2 group substituted with a group selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy;

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carboxylic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy, or a C_1-C_2 group substituted with a group selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy; and

R is CXR'.

29. A method according to any one of claims 26 to 28 wherein Z of at least one of M and M' is other than a 2,3-disubstituted carbocyclic group.

30. A method according to any one of claims 26 to 29 wherein Z of at least one M and M' comprises:

at least two substituents ortho relative to one another or in adjacent substitution positions when the Z group is selected from (d) and W is CH or a C_1-C_3 linker group; or

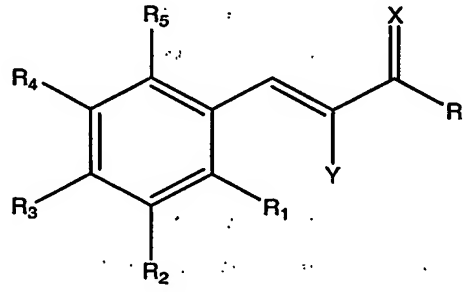
the, or one of, the substituents on a carbon atom adjacent to the, or one of the, heteroatom(s) when the Z group is a heterocyclic group selected from (c); or

when W, V and Y are cyclised forming a heterocyclic ring fused with Z, the, or

one of, the substituents on a carbon atom of Z spaced at least one bond length from the heterocyclic ring.

31. A method according to any one of claims 26 to 30 wherein when the Y substituent of one of M or M' is hydrogen, the Y substituent of the other of M and M' is other than hydrogen.

32. A method according to any one of claims 26 to 31 wherein M and M' are each independently a moiety as follows:



wherein:

X is O or S;

Y is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, or thiocarboxy; or

R_1 and Y are cyclised forming a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring, wherein the heterocyclic ring includes 1 or 2 heteroatoms selected from O,N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R_2 to R_5 are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, C_1-C_2 alkoxy and C_1-C_2 acyl; or

R_1 to R_5 are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, halo, C_1-C_2 alkoxy and C_1-C_2 acyl; and

R is NH, O is S bonded to the spacer Sp; and

wherein at least one of M and M' is characterised in that, at least two of R_1 to R_5 are other than hydrogen and when R_1 to R_2 are other than hydrogen at least one of R_3 to R_5 is also other than hydrogen, or when R_1 and Y are cyclised, at least two of R_2 to R_5 are other than hydrogen when R_1 and Y form an unsubsituted carbocyclic group

or at least one of R_2 to R_5 is other than hydrogen when Y and R_1 form a heterocyclic group.

33. A method according to claim 32 wherein R_1 to R_3 are other than hydrogen.

34. A method according to any one of claims 26 to 31 wherein at least two of R_1 to R_5 are in ortho positions relative to one another.

35. A method according to any one of claims 26 to 31 wherein at least one of M and M' has three substituents and wherein the substituents are adjacent to one another.

36. A method according to claim 33 wherein either R_1 to R_3 are other then hydrogen or R_2 to R_5 are other than hydrogen.

37. A method according to any one of claims 26 to 32 wherein when at least one of R_1 to R_5 or R_2 to R_5 is halo, C_1-C_2 alkoxy or C_1-C_2 acyl, at least one other substituent is selected from nitro, amino, hydroxy, carboxy and thiocarboxy when R_1 and Y are cyclised and form a heterocyclic ring, or at least two other substituents are selected from nitro, amino, hydroxy, carboxy and thiocarboxy when R_1 and Y are not cyclised or form an unsubstituted carboxylic ring.

38. A method according to any one of claims 26 to 37 wherein Y is cyano, X is O and R is NH.

39. A method according to any one of claims 26 to 38 wherein M and M' are the same.

40. A method according to any one of claims 26 to 39 wherein the spacer Sp permits the compound to adopt a hairpin conformation.

41. A method according to any one of claims 26 to 40 wherein the compound of formula I is a dimeric tyrphostin.

42. A method according to any one of claims 26 to 41 wherein the disease or condition is selected from the group consisting of cancers, ophthalmologic diseases, immunodeficiency diseases, gastrointestinal diseases, pathogenic infections, kidney diseases, epilepsy, and neurological, neurodegenerative and nervous system diseases and conditions.

43. A method according to claim 42 wherein the neurological, neurodegenerative and nervous system diseases and conditions are selected from the group consisting of

demyelinating diseases, Alzheimer's disease, Huntington's disease, Parkinson's disease and Lewy body diseases.

44. A method according to claim 42 wherein the disease or condition is epilepsy.

45. A method for prophylaxis or treatment of a disease or condition in a mammal mediated by dynamin-dependent endocytosis, the method comprising administering to the mammal an effective amount of a dimeric tyrphostin which inhibits GTPase activity of dynamin, or an analogue, physiologically acceptable salt, or prodrug of the dimeric tyrphostin.

46. A method according to claim 45 wherein the dimeric tyrphostin comprises two tyrphostin moieties linked together by a spacer moiety, wherein at least one of the tyrphostin moieties is a benzylidenemalonitrile moiety.

47. A method according to claim 46 wherein both of the tyrphostin moieties are benzylidenemalonitrile moieties.

48. A method according to claim 46 or 47 wherein the tyrphostin moieties are the same.

49. A method according to any one of claims 45 to 48 wherein the dimeric tyrphostin comprises bis-tyrphostin.

50. A method according to any one of claims 45 to 49 wherein the disease or condition is selected from the group consisting of cancers, ophthalmologic diseases, immunodeficiency diseases, gastrointestinal diseases, pathogenic infections, kidney diseases, epilepsy, and neurological, neurodegenerative and nervous system diseases and conditions.

51. A method according to claim 50 wherein the neurological, neurodegenerative and nervous system diseases and conditions are selected from the group consisting of demyelinating diseases, Alzheimer's disease, Huntington's disease, Parkinson's disease and Lewy body diseases.

52. A method according to claim 50 wherein the disease or condition is epilepsy.

53. A method for identifying a dimeric tyrphostin or an analogue thereof with ability to inhibit GTPase activity of dynamin, the method comprising:

incubating the dimeric tyrphostin or analogue thereof with dynamin or a molecule having dynamin GTPase activity to provide test data; and

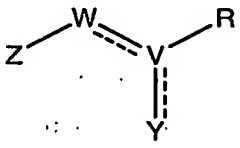
determining whether the dimeric tyrphostin or analogue thereof inhibits the GTPase activity of dynamin on the basis of the test data.

54. Use of a dimeric tyrphostin or analogue thereof identified by a method as defined in claim 53 to inhibit dynamin-dependent endocytosis in cells.

55. A compound of Formula III or a physiologically acceptable salt, or prodrug thereof, wherein:

M-Sp-M' **Formula III**

M and M' are each independently a moiety of formula IV and are the same or different, and Sp is a spacer.



Formula IV

V is C or CH;

W is CH or a linker group; and

Y is hydrogen, cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubsituted C_1-C_3 group or C_1-C_3 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or the heterocyclic ring, when substituted, has at least one substituent selected from cyano, NH, nitro, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubsituted C_1-C_3 group or C_1-C_3 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH_2R', CXR' or CHX'R';

X is O or S;

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubsituted C_1-C_3 group or C_1-C_3 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur;

R' is NH, O or S bonded to the spacer; and

Z is selected from:

(a) an unsubstituted heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S;

(b) an unsubstituted carbocyclic group consisting of one or two rings independently having 5 or 6 ring members;

(c) a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S, wherein the heterocyclic group has one or more substituents independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl; and

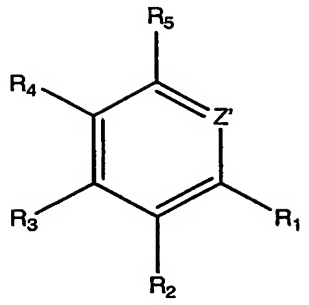
(ii) a C_1-C_2 alkyl or C_1-C_2 alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl; and

(d) a carbocyclic group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents when W is CH or a linker group or W, V and Y form an unsubstituted carbocyclic group, or at least one substituent when W, V and Y form a heterocyclic group, independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl; and

(ii) a C_1-C_2 alkyl or C_1-C_2 alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C_1-C_2 alkoxy and C_1-C_2 acyl;

wherein when Z of one of M or M' is selected from (b), Z of the other of M or M' is selected from (a), (c) or (d), and with the proviso that Z of at least one of M and M' is other than a benzyl group of formula IVa when R is CXR', X is O, R' is NH bonded to the spacer, V is C, W is CH, Y is cyano, and



Formula IVa

R_1, R_2, and R_5 are H, and R_3 and R_4 are hydroxy; or

R_1 and R_5 are H, and R_2 to R_4 are hydroxy when Sp is a C_2-C_4 alkyl spacer; and

wherein Z' is a carbon atom bonded to W.

56. A compound according to claim 55 wherein:

V is C;

W is CH;

Y is hydrogen, cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C_1-C_2 group or C_1-C_2 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur, or an unsubstituted C_1-C_2 group or C_1-C_2 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH_2R', CXR' or CHX'R';

X is O or S; and

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C_1-C_2 group or C_1-C_2 group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulphur.

57. A compound according to claim 56 wherein:

Y is cyano, nitro, amino, carboxy, hydroxy, sulfhydryl, thiocarboxy, or a C_1-C_2

group substituted with a group selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy;

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carboxylic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy, or a C_1-C_2 group substituted with a group selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy; and

R is CXR'.

58. A compound according to any one of claims 55 to 57 wherein Z is selected from:

(i) a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms independently selected from O, N and S;

(ii) a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms independently selected from O, N and S, wherein the heterocyclic group has one or more substituents independently selected from nitro, NH, halo, cyano, amino, hydroxy, carboxy, oxo, sulfur, and C_1-C_2 alkoxy; and

(iii) an carbocyclic group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents independently selected from nitro, NH, amino, halo, cyano, hydroxy, carboxy, oxo, sulfur and C_1-C_2 alkoxy.

59. A compound according to any one of claims 55 to 58 wherein Z of at least one of M and M' is other than a 2,3-disubstituted carboxycyclic group.

60. A compound according to any one of claims 55 to 59 wherein Z of at least one of M and M' comprises:

at least two substituents in ortho positions relative to one another or in adjacent substitution positions, when the Z group is selected from (d) and W is CH or a C_1-C_3 linker group; or

the, or one of, the substituents on a carbon atom adjacent to the, or one of the, heteroatom(s) when the Z group is a heterocyclic group selected from (c); or

when W, V and Y are cyclised forming a heterocyclic ring fused with Z, the, or one of, the substituents on a carbon atom spaced at least one bond length from the heterocyclic ring.

61. A compound according to any one of claims 55 to 60 wherein when the Y substituent of one of M or M' is hydrogen, the Y substituent of the other of M and M' is other than hydrogen.

62. A compound according to any one of claims 55 to 61 wherein W, V and Y form a 5 or 6 membered heterocyclic ring fused with Z.

63. A compound according to claim 62 wherein the heterocyclic ring fused with Z forms a two ring heterocyclic group.

64. A compound according to any one of claims 55 to 63 wherein Z comprises an aryl group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents independently selected from nitro, NH, amino, halo, cyano, hydroxy, carboxy, oxo, sulphur and C_1-C_2 alkoxy.

65. A compound according to claim 64 wherein Z comprises an aryl group consisting of one ring having 6 ring members and at least two substituents independently selected from nitro, amino, halo, cyano, hydroxy, carboxy and C_1-C_2 alkoxy.

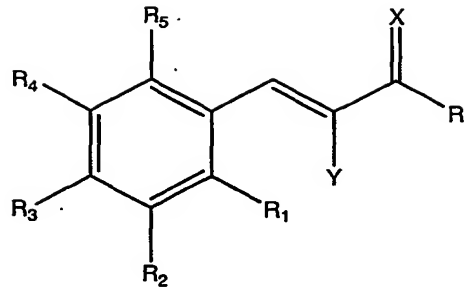
66. A compound according to claim 65 wherein the aryl group has at least two substituents independently selected from nitro, amino, and hydroxy.

67. A compound according to any one of claims 55 to 62 wherein Z comprises a heterocyclic group having one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S, wherein the heterocyclic group has one or more substituents independently selected from nitro, NH, halo, cyano, amino, hydroxy, carboxy, oxo, sulphur and C_1-C_2 alkoxy.

68. A compound according to claim 67 wherein the heterocyclic group has one or more substituents independently selected from nitro, amino and hydroxy.

69. A compound according to any one of claims 55 to 59 wherein M and M' are each independently a moiety as follows:

69.



wherein:

X is O or S;

Y is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, or thiocarboxy; or

R_1 and Y are cyclised forming a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring, wherein the heterocyclic ring includes 1 or 2 heteroatoms selected from O,N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R_2 to R_5 are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, C_1-C_2 alkoxy and C_1-C_2 acyl; or

R_1 to R_5 are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, halo, C_1-C_2 alkoxy and C_1-C_2 acyl; and

R is NH, O is S bonded to the spacer Sp; and

wherein at least one of M and M' is characterised in that, at least two of R_1 to R_5 are other than hydrogen and when R_1 to R_2 are other than hydrogen at least one of R_3 to R_5 is also other than hydrogen, or when R_1 and Y are cyclised, at least two of R_2 to R_5 are other than hydrogen when R_1 and Y form an unsubsituted carbocyclic group or at least one of R_2 to R_5 is other than hydrogen when Y and R_1 form a heterocyclic group.

70. A compound according claim 69 wherein R_1 to R_3 are other than hydrogen.

71. A compound according to claim 69 wherein at least two of R_1 to R_5 are in ortho positions relative to one another.

72. A compound according to claim 69 wherein at least one of M and M' has three substituents and wherein the substituents are adjacent to one another.

73. A compound according to claim 72 wherein either R_1 to R_3 are other then hydrogen or R_2 to R_5 are other than hydrogen.

74. A compound according to claim 69 wherein when at least one of R_1 to R_5 or R_2 to R_5 is halo, C_1-C_2 alkoxy or C_1-C_2 acyl, at least one other substituent is selected from nitro, amino, hydroxy, carboxy and thiorcarboxy when R_1 and Y are cyclised and form a heterocyclic ring, or at least two other substituents are selected from nitro, amino, hydroxy, carboxy and thiocarboxy when R_1 and Y are not cyclised or form an unsubstituted carboxylic ring.

75. A compound according to any one of claims 69 to 74 wherein Y is cyano, X is O and R is NH.

76. A compound according to any one of claims 55 to 75 wherein M and M' are the same.

77. A compound according to any one of claims 55 to 76 wherein the spacer Sp permits the compound to adopt a hairpin conformation.

78. A compound according to any one of claims 55 to 77 wherein the spacer Sp comprises an unsubstituted alkane chain as follows:

$$-CH_2(CH_2)_nCH_2-$$

wherein n is an integer of from 1 to 5.

79. A compound according to any one of claims 1 to 78 wherein the compound of Formula III is a dimeric tyrphostin.

80. A pharmaceutical composition comprising a compound as defined in any one of claims 55 to 58 together with a physiologically acceptable excipient, carrier or diluent.